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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,928	03/23/2005	Marc Hubert Mercken	PRD-0032-USPCT1	4646

27777 7590 05/27/2010

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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
05/27/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/528,928	MERCKEN ET AL.	
	Examiner	Art Unit	
	CHANG-YU WANG	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-25,28 and 31-36* is/are rejected.

7)☒ Claim(s) *26,27,29 and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. The Applicant Initiated Interview request filed on 2/16/10 was dismissed because Applicant did not participate in the scheduled phone interview on 3/8/10. Applicant requested to reschedule another interview at another time. However, the examiner and Applicant did not have an agreement with another scheduled interview. Thus, the Applicant initiated interview request filed on 2/16/10 was dismissed.

2. Applicant's amendment filed 2/16/10 is acknowledged. Claims 1-16 are cancelled. Claims 18-19 are amended. Claims 17-36 are pending in this application and under examination in this office action.

3. Applicant's arguments filed on 2/16/10 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

4. The rejection of claims 18 and 19 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in response to Applicant's amendment to the claims.

Claim Rejections/Objections Maintained

In view of the amendment filed on 2/16/10, the following rejections are maintained.

Claim Rejections

5. Claims 18 and 19 are objected to because of the following informalities: the status of the claims 18-19 are incorrect because these claims have been amended. Appropriate correction is required.

See MPEP 714 & 37 CFR 1.121.
"In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered)."

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-19, 22-23, 28 and 36 stand rejected under 35 U.S.C. 102 (b) as being anticipated by Walker et al (J. Neuropathol. Exp. Neurol.1994 Jul. 53: 377-383), Pirttila et al. (J. Neurol Sci. 1994 Dec 1; 127:90-5), WO0162801 (as in IDS submitted on Mar 23, 2005) or Naslund et al (as in IDS submitted on Mar 23, 2005). Claims 17-19, 22-23, 28 and 36 (original claim 35) are rejected under 35 U.S.C. 102 (b) as being anticipated by Solomon et al. (Proc. Natl. Acad. Sci. USA. 1996. 93: 452-455). Claims 17-19, 22-23, 28 and 36 (original claim 35) are rejected under 35 U.S.C. 102 (a) as being anticipated by Huse et al. (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284). These rejections are maintained for the reasons made of record and the reasons set forth below

Claims 17-19, 22-23, 28 and 36 as amended are drawn to a monoclonal antibody which specifically binds to an Aβ11-x polypeptide at one or more epitopes present on the first 5-7 N-terminal amino acids, wherein the antibody does not specifically bind to a full length Aβ1-40/42 peptide and a hybridoma of the claimed antibody.

On p. 5-10 of the response, Applicant argues that none of the cited references dislcose the claimed antibody that binds to one or more epitopes on the first 5-7 N-terminal amino acids of Aβ11-x, binds specifically to Aβ11-x and do not specifically bind to a full length Aβ1-40/42 peptides as presently claimed. Applicant argues that none of the art provides motivation to modify the antibodies of Huse to arrive at the claimed antibodies. Applicant argues that one of Huse's antibodies, BNT77, binds to Abeta11-16 and Abeta11-x but it teaches away from the claimed antibodies because it bind to full length Abeta1-40/42. Applicant argues that Walker and WO01/62801 are silent as to whether the antibodies therein specifically bind to Abeta11-x peptides and that the antibodies disclosed by Walker and WO01/62801 bind to full length Abeta1-40/42 peptides. Applicant's arguments have been fully considered but they are not persuasive.

In response, as previously made of record, the art antibodies were raised against Aβ1-16 (10D5 & 6E10, Walker and Naslund), Aβ17-24 (4G8, Prittila), and Aβ13-28 (266, WO01/62801) immungens and thus can bind to the epitopes of Aβ11-x including the epitopes on the first 5-7 amino acids as evidenced by Huse et al (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284, cited in the previuos office action). In addition, the

antibodies raised against Aβ 1-28 and 8-17 taught by Solomon would inherently recognize Aβ11-x because the amino acid sequence of the immunogens (5-7 amino acids of Aβ11-x) for the instant antibodies are encompassed within the sequences of amino acids 1-28 and 8-17 of Aβ.

For the same reason, the antibody BNT77 taught by Huse et al. was raised against amino acids 11-16 of Aβ, thus it can recognize Ab11-x at one or more epitopes on the first 5-7 N-terminal amino acids including Aβ11-15 amd Aβ11-17 that are used to raise the claimed antibody. If the epitopes to which Applicant's antibody binds are present in Aβ11-x, so that Applicant's antibody binds to Aβ11-x, these epitopes are also present in Aβ11-16, 1-28 and 8-17, which were used to generated the antibodies diclosed by the prior art references.

With regard to whether the art antibodies have the same property as the claimed antibodies that bind to Aβ11-x without specifically binding to the full length of Aβ1-40/42, it is noted that Applicant claims a product in terms of a function, property or characteristics is the same as the prior art products. Note that

"Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.' In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See MPEP § 2112.01 [R-3].

As previuosly made of record, if the epitopes to which Applicant's antibody binds are present in Aβ11-x, so that Applicant's antibody binds to Aβ11-x, these epitopes are also present in Aβ 1-16, 17-24, and 13-28.

In addition, it is known in the art that anti-Aβ antibodies can cross react with different species or different lengths of Aβ peptides in different titrations because of their different binding affinity. Applicant has provided no showing that the antibodies in the art have characteristics different from those specified by Applicant and thus do not cross react with the full length of Aβ1-40/42 under the same titration or concentration and under the same incubation conditions as those of the prior art. Note that Applicant fails to provide side-by-side comparisons to demonstrate that the claimed antibody is different from those antibodies disclosed by Walker et al., Pirtila, WO0162801, Naslund and Huse.

Since the claimed antibody is substantially identical to the art antibodies in structure or composition and is able to bind to Aβ11-x, the antibodies disclosed by Walker et al., Pirtila, WO0162801, Naslund and Huse farily anticipate the claimed antibody because Applicant fails to demonstrate that the claimed antibody has a function, property or characteristics different from the antibodies dislcosed by the art.

Accordingly, the rejection of claims 17-19, 22-23, 28 and 36 under 35 U.S.C. 102 (b) as being anticipated by Walker et al., Pirttila et al., WO0162801 or Naslund et al. is maintained. The rejection of claims 17-19, 22-23, 28 and 36 (original claim 35) under 35 U.S.C. 102 (b) as being anticipated by Solomon et al. or by Huse et al. is maintained.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17-25, 28 and 31-36 stand rejected under 35 U.S.C. 103(a) for being unpatentable over Huse et al. (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284) in view of Walker et al (J. Neuropathol. Exp. Neurol.1994 Jul. 53: 377-383) and WO0162801. The rejection is maintained for the reasons made of record.

Claims 17-25, 28 and 31-36 as amended are drawn to a monoclonal antibody which specifically binds to a Aβ11-x polypeptide at one or more epitopes present on the first 5-7 N-terminal amino acids, wherein the antibody does not specifically bind to a full length Aβ1-40/42 peptide, a hybridoma of the claimed antibody and methods of detecting Aβ11-x peptide in a sample or diagnose AD by detecting and comparing the amount of Aβ11-x in a test sample and a control.

On p. 11 of the response, Applicant argues that all of the antibodies disclosed by Huse lack one or more properties of the claimed antibodies. Applicant argues that none of the art provides motivation to modify the antibodies of Huse to arrive at the claimed antibodies. Applicant argues that Huse teaches away from the claimed invention because Huse teaches an antibody produced with the first 5-7 N-terminal amino acids of Aβ11-x (i.e. Aβ11-16 immunogen) would also bind to the full length Aβ1-40/42. Applicant aruges that both Walker and WO0162801 are silent as to whether the disclosed antibodes bind to Aβ11-x and thus cannot cure the deficiency in Huse. Applicant's arguments have been fully considered but they are not persuasive.

In response, for the reasons set forth above in section of the 102 rejection at paragraph 7, the antibodies disclosed by Huse et al., Walker et al. and WO0162801 do recognize Aβ11-x because the antibodies disclosed by Huse et al., Walker et al. and WO0162801 have been shown to have the same property as that of the claimed antibodies.

In addition, the examiner asserts that Huse does not teach away from the claimed invention because the antibody disclosed by Huse was raised against Aβ11-16, which meets the limitation of the claim 17. Note that the claimed antibodies were raised against Aβ11-15 amd Aβ11-17. Thus, the antibody raised against Aβ11-16 would have similar property as the antibodies raised against Aβ11-15 amd Aβ11-17.

Note that Applicant cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

WO0162801 was cited to support the limitations recited in claims 24-25, 28 and 36. WO0162801 teaches hybridoma, humanized and chimeric antibodies and a diagnostic composition comprising the claimed antibodies as in claims 24-25, 28 and 36 (original claim 35). WO0162801 also teaches a method of detection of Aβ in the brain tissue and CSF of Alzheimer's disease patients using labeled antibodies by electrophoresis or ELISA as recited in instant claims 20-21 and 31-35 (including duplicate claim 34) (see p.26, examples 1-2; p. 30, example 6, in particular). Thus, It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to use the antibody raised against Aβ11-16 or use the antibody that can recognize Aβ11-x to detect Aβ11-x in Alzheimer's disease because the level of Aβ11-40/42 has been shown increased in AD patients. The person of ordinary skill in the art would have been motivated do so with an expectation of success in using an antibody that recognize Aβ11-x to detect diseases associated Aβ formation because the antibody against Aβ11-16 is able to detect Aβ11-40/42 in AD brains. Accordingly, the rejection of claims 17-25, 28 and 31-36 under 35 U.S.C. 103(a) for being unpatentable over Huse et al. in view of Walker et al. and WO0162801 is maintained.

Conclusion

Allowable Subject Matter

8. Claims 26-27, 29 and 30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Claims 17-25, 28 and 31-36 are rejected.

10. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
May 13, 2010

/Christine J Saoud/
Primary Examiner, Art Unit 1647